REMARKS

Claims 1-9 and 25-29 were pending in this application at the time the above identified Office action was mailed. Claim 1 has been amended. Support for the amended claim comes from at least pages 14, lines 12-16 and page 11, lines 3-31.

The following remarks are numbered to correspond to the numbering used in the referenced Office action (Paper Number 13).

2-3. The Provisional Obviousness Double Patenting Rejection

The Office has provisionally rejected claims 1-9 and 25-29 under the judicially created doctrine of obviousness type double patenting as being unpatentable of claims 1-7, 10-16, 20, 35-39 and 41-44 of copending application serial no. 09/183824.

No action is believed required by Applicant as the alleged conflicting claims have not in fact been patented.

4-5. The Rejection of the Claims under 35 U.S.C. 102(b)

The Office has rejected claims 1-5 and 25 under 35 U.S.C. 102(b) as being anticipated by Kumpel et al., (1994) Hum. Antib. Hybridomas 5(3 and 4):143-151 (Kumpel). The Office contends that Kumpel teaches human monoclonal antibodies wherein substantially all of the oligosaccharide is a G2 oligosaccharide referring to Table 1 and columns 1-3 at page 149 of Kumpel. The Office states that the "preparations are substantially homogenous for the glycoprotein because they contain monoclonal antibodies in serum free tissue culture medium." (Paper 13, page 3). The Office further contends that Applicant's claims and specification do not disclose the degree of purity associated with the term "substantially all." Applicants respectfully traverse.

As Applicants have previously noted, Kumpel describes a monoclonal antibody, 2B6, produced from an EBV-transformed B-lymphoblastoid cell line and alleged to contain 78.7% digalactosyl oligosaccharides, 17.7% monogalactosyl oligosaccharides and 3.6% agalactosyl oligosaccharides after

chemical removal of terminal sialic acid residues. (Table 1 and accompanying text, page 145, Kumpel). Table 1 of Kumpel also shows that 21.7 % of the oligosaccharides in the original preparation are sialylated (Table 1 and text at page 146). According to Kumpel, a substantial portion (21.7%) of the galactosylated oligosaccharides (some combination of either mono- or digalactosylated) terminate in a sialic acid residue and not galactose residue. Therefore the 2B6 antibody preparation described is not a substantially homogenous glycoprotein preparation wherein substantially all of the oligosaccharide is a G2 oligosaccharide. In fact, the 2B6 preparation is a heterogenous mixture of several different glycoforms, typical of the preparations of the prior art.

Applicants disagree that the specification fails to define the degree of purity associated with the limitation "substantially all," as that term is clearly used in the context of the present invention to refer to a composition substantially free of glycoproteins comprising an immunoglobulin CH2 domain wherein the N-linked oligosaccharide is a G1 or G0 oligosaccharide (see, for example, page 6, lines 1-4). The term "substantially" is defined at, for example, page 14, lines 3-9,

> to indicate that the product is substantially devoid of by-products originated from undesired glycoforms (*e.g.* G0 and G1). Expressed in terms of purity, substantial homogeneity means that the amount of by-products does not exceed 10%, and preferably is below 5%, more preferably below 1%, most preferably below 0.5%, wherein the percentages are by weight.

As discussed above, Kumpel describe a preparation containing 78.7% digalactosyl oligosaccharides, 17.7% monogalactosyl oligosaccharides and 3.6% agalactosyl oligosaccharides <u>after</u> chemical removal of terminal sialic acid residues and therefore cannot anticipate the claims as drafted.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the pending rejection of the

claims under 35 USC 102(b).

In an effort to advance allowance of the subject matter of the claims, Applicants have amended claim 1 to further recite that the amount of said glycoprotein containing oligosaccharide terminating in sialic acid does not exceed 10% by weight of the preparation. This further distinguishes Kumpel which shows that 21.7 % of the oligosaccharides in the original preparation are sialylated (Table 1 and text at page 146).

6-7. The Rejection of the Claims under 35 U.S.C. 103(a)

The Office has rejected claims 1-9 and 25-29 under 35 U.S.C. 103(a) as being unpatentable over Kumpel, in view of US patent 5,834,251 by Maras et al. (Maras et al.). The Office contends that Kumpel teach that antibodies with substantially all G2 oligosaccharide have increased lysis of target cells in comparison the same antibody which is produced in a manner that results in low levels of G2. The Office further contends that Maras et al. teach that a galactosyltransferase enzyme can be used to modify the oligosaccharide profile on a glycoprotein while relying on the specification for disclosure of clinical uses of various antibodies. Applicants respectfully traverse.

As discussed in the previous section Kumpel do not describe or suggest a composition comprising a glycoprotein wherein substantially all of the oligosaccharide is a G2 oligosaccharide. Importantly, Kumpel do not describe increased lysis of target cells for an antibody after chemical removal of the sialic acid residues. The activity data described by Kumpel is for a heterogenous glycoprotein preparation and not a composition wherein substantially all of the oligosaccharide is a G2 oligosaccharide. In fact, as described above almost 22 % of the galactosylated oligosaccharides detected by Kumpel terminated in a sialic acid residue. Therefore Kumpel alone or in combination with Maras et al. fail to provide the motivation to produce Applicant's claimed compositions but rather suggest only that

some heterogenous glycoprotein preparation can be prepared.

To view the combinations of disclosures to suggest a substantially homogenous preparation as claimed relies on impermissible hindsight analysis in view of the teaching offered only by Applicant since none of the describe or suggest a substantially homogenous preparation be prepared.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the pending rejection of the claims under 35 U.S.C. 103.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."** Also attached is a clean set of all pending claims for ease of reference.

CONCLUSION

Applicants respectfully request that the foregoing amendments be considered and entered in the file history of the above-identified application. It is submitted that the claims are now in condition for allowance. It is therefore earnestly solicited that such a final favorable disposition is made. The Examiner is invited to telephone Jeffrey S. Kubinec, (Reg. No. 36,575) at (650) 225-8228 if deemed helpful to clarify and advance prosecution.

Respectfully submitted,
GENENTECH, INC.

Date: April 24, 2001 By: _____
Jeffrey S. Kubinec
Reg. No. 36,575
Telephone No. (650)225-8228

"**Version with Markings to Show Changes Made**"

In the claims:

Claim 1 has been amended as follows:

1. (amended) A composition comprising a substantially homogenous glycoprotein preparation, said glycoprotein having an immunoglobulin CH2 domain said CH2 domain having at least one N-linked oligosaccharide wherein substantially all of the oligosaccharide is a G2 oligosaccharide and wherein the amount of said glycoprotein containing a G1 or G0 oligosaccharide does not exceed 10% by weight of the preparation.